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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/894.806	06/28/2001	Alan L. Greener	25436/1712	4116

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EXAMINER

MARVICH, MARIA

ART UNIT	PAPER NUMBER
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1636

DATE MAILED: 08/13/2002

8

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.		Applicant(s)	
	09/894,806		GREENER ET AL.	
	Examiner		Art Unit	
	Maria B. Marvich		1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-3,5-41,43,45-74 and 78-80 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 4,42,44 and 75-77 is/are allowed.
- 6) ☒ Claim(s) 1-3,5-41,43,45-74 and 78-80 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on ____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. ____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). ____. |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) <u>4</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Claim Objections

Claims 56 and 57 are objected to under 37CFR 1.75 as being duplicates of one another. Appropriate correction is required.

Specification

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code on page 11. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 22, 23, 28, 63, rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 22 recites the limitation "said glass-forming matrix material" in 18. There is insufficient antecedent basis for this limitation in the claim.

Claim 23 recites the limitation "said at least one carbohydrate" in 19. There is insufficient antecedent basis for this limitation in the claim.

Claims 28 and 63 contain the trademark/trade name ficoll. Where a trademark or trade name is used in a claim as a limitation to identify or describe a particular material or product, the

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claim does not comply with the requirements of 35 U.S.C. 112, second paragraph. See *Ex parte Simpson*, 218 USPQ 1020 (Bd. App. 1982). The claim scope is uncertain since the trademark or trade name cannot be used properly to identify any particular material or product. A trademark or trade name is used to identify a source of goods, and not the goods themselves. Thus, a trademark or trade name does not identify or describe the goods associated with the trademark or trade name.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-3, 5-8, 16-41, 47-55, 58-74 are rejected under 35 U.S.C. 102(b) as being anticipated by Bronshtein et al. WO 99/27071 (June 3, 1999)

Bronshtein et al. teach a method of generating storage stable XL10 gold competent cells, *E. coli* gram negative cells that are generated by exposure to buffer containing CaCl_2 , that comprises drying cells above freezing for at least 8 hours (page 11, line 2-3) in a vacuum under non-atmospheric pressure (page 10, line 23-25). Bronshtein et al. use a preservation solution consisting of 25% sucrose and 25% fructose and the cells are dried at a single uniform temperature (room temperature) under vacuum and then stored at room temperature for 24 days (page 7, line 31-34). According to the disclosure of the invention, temperatures ranging from 0-100°C are used for drying purposes (page 2, line 18). Additionally, protectants that can be used

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include sucrose, ficoll, polyethylene glycol, trehalose, sorbitol, polyacrylamide, and combinations thereof (page 5, line 17-24).

Bronshtein et al. also teach the use of Tg (glass-transition temperature) values in storage determination. According to Bronshtein (page 2, line 21-26) a secondary drying under vacuum in the range of 0-100°C for periods of time sufficient to increase the glass transition temperature to a point above the selected storage temperature within the range of 0 °C -70 °C is necessary to provide long-term shelf preservation of biological suspensions in the glass state. Therefore, the Tg desired can be achieved by manipulating drying time and temperature; a Tg of a matrix-cell mixture greater than 15°C (as recited in the instant application in claim 47) is achieved by drying the matrix-cell mixture at 25 °C for 40+ hours (figure 2). This can be reasonably accomplished for any choice of protectant used for cell drying. According to the Figure 3, at least 30% of the cells are viable following rehydration.

Claims 1-3, 6-12, 15-16, 19-21, 23-28, 31, 43, 45-46 are rejected under 35 U.S.C. 102(b) as being anticipated by Jessee et al. WO 98/35018 (August 13, 1998).

Jessee et al. teach a method of generating storage stable competent cells that comprises drying cells above freezing (to 10 °C) for at least 8 hours (page 11, line 2-3) in a vacuum under non-atmospheric pressure (page 10, line 23-25). The competent cells are preferably E. coli (page 6, line 5-24) and are made competent in a buffer containing CaCl₂ (page 8, line 11-14). The cells are storage stable for at least 45 days at temperatures ranging from 4 °C to -80 °C with a transformation efficiency of at least $1(10)^5$ (page 11, line 6-20). Jessee et al. teach the use of glass forming cryoprotectants (and combinations of) that include carbohydrates such as

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trehalose, sucrose, sorbitol, PVP, ficoll. Also provided is a method for transforming nucleic acids utilizing the components of the invention following rehydration of the cells in transformation buffer in which cells exhibit at least $1(10)^5$ transformants/mg DNA (page 12, 1-20).

(e) the invention was described in-

(1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effect under this subsection of a national application published under section 122(b) only if the international application designating the United States was published under Article 21(2)(a) of such treaty in the English language; or

(2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a).

Claims 1-3, 6-17, 21, 24, 29, 43, 45 and 46 are rejected under 35 U.S.C. 102(e) as being anticipated by Barnea et al. US application 2002/0081565.

Barnea et al. teach a method for generating storage-stable competent cells that are also transformed with exogenous DNA. In example 1 and 2, E.coli cells are made competent in CB-I buffer comprised of CaCl_2 and sucrose or trehalose (page 5, [0059]). The cells were lyophilized at 0°C for 10 hours, 5°C , 10°C , 15°C , 20°C and 25°C for 30 minutes each in CB-I buffer with sucrose or trehalose. In example 3, the cells were stored at -70°C , -20°C , and 4°C for 28 days with at least $(10)^5$ transformants/ μg DNA (page 8, table 5). Cells to be transformed are rehydrated in buffer used for the transformation (transformation buffer) and exhibit at least $(10)^5$ transformants/ μg DNA (page 5, [0057] and table 2). A variety of cryoprotectants are anticipated by the invention including the polyol inositol, galactose, glucose, lactose, sucrose and trehalose (page 3, [0033]).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 47-63, and 78-80 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jessee et al. WO 98/35018 in view of Bronshtein et al. WO 99/27071.

Applicant claims a composition comprising a glass forming matrix and competent cells wherein the glass transition temperature of the matrix-cell mixture is greater than 15- 60 °C and maintains a transformation efficiency of at least $1(10)^5$ transformants/mg DNA. The glass-forming matrix includes carbohydrates and polymers such as trehalose, sucrose, ficoll, polyethylene glycol and combinations thereof. As well as method of producing recombinant polypeptides using the cells of the invention are recited that includes methods for sorting transformed and untransformed cells as well as isolating the polypeptide.

Jessee et al. teach the use of glass forming cryoprotectants (and combinations of) that include carbohydrates such as trehalose, sucrose, sorbitol PVP, ficoll wherein cells exhibit at least $1(10)^5$ transformants/mg DNA (page 12, 1-20). At lest 30% of the cells are viable upon rehydration (page 11, 25-30. Included is a method for producing a polypeptide (page 12, line 26-29) and for the separation of cells based upon uptake of nucleic acids (page 13, line 12-14) and the recombinant polypeptide is isolated (page 13, line 15-18). Jessee et al. do not teach how to determine nor do they give Tg values for the cryoprotectants used.

Bronshtein et al. also teach the use of Tg values in storage determination. According to Bronshtein (page 2, line 21-26) a secondary drying under vacuum in the range of 0-100°C for periods of time sufficient to increase the glass transition temperature to a point above the selected storage temperature within the range of 0 °C -70 °C is necessary to provide long-term shelf preservation of biological suspensions in the glass state. Therefore, the Tg desired can be achieved by manipulating drying time and temperature; a Tg of a matrix-cell mixture greater than 15°C (as recited in the instant application in claim 47) is achieved by drying the matrix-cell mixture at 25 °C for 40+ hours (figure 2). This can be reasonably accomplished for any choice of protectant used for cell drying.

A person of ordinary skill in the art would have been motivated to combine the teachings of Bronshtein regarding guidelines for determining the Tg values of the cryoprotectants required for the development of the storage stable competent cells for the successful use of the competent cells for polypeptide production. It would have been obvious to someone of skill in the art to utilize Tg values for determining the time and duration due to the success in the art of these temperatures in predicting stability of biological material under long-term storage. To transform nucleic acids and generate recombinant polypeptide according to Jessee et al. successful long term storage techniques are required. Given the teachings of the cited art and the level of skill of the ordinary skilled artisan at the time of the applicant's invention, it must be considered that said ordinary skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

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Claims 4, 42, 75-77 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maria B Marvich, PhD whose telephone number is (703) 605-1207. The examiner can normally be reached on M-F (6:30-3:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, PhD can be reached on (703) 305-1998. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 305-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the patent analyst, Kay Pinkney, whose telephone number is (703) 305-3553.

Maria B Marvich, PhD
Examiner
Art Unit 1636

August 9, 2002


DAVID GUZO
PRIMARY EXAMINER